Purine nucleoside phosphorylase deficiency

GENERAL INFORMATION

Description:

Defects in NP are the cause of a severe T-cell immunodeficiency with neurologic disorder in children. It is an autosomal recessive disorders with decreased T cells and lymphopenia and antibody deficiency. The enzyme deficiency result in accumulation of toxic metabolites for T-cell development.

Alternative names:

- PNP
- Nucleoside Phosphorylase Deficiency
- Ataxia with deficient cellular immunity

Classification:

- Combined B and T cell immunodeficiencies
  - Deficiencies of purine metabolism

Inheritance:

Autosomal recessive

OMIM:

- #202500 Severe combined immunodeficiency 1, SCID1
- +164050 Nucleoside phosphorylase; NP

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for ADA deficiency

Incidence:

1:54,000 (Switzerland) to 1:200,000 (Japan)

CLINICAL INFORMATION

Description:

The clinical presentation of PNP deficiency includes reccurent infections of the upper and lower respiratory tract due to common bacterial pathogens, viruses, or opportunistic infections such as Candida albicans and Pneumocystis carinii. Infections typically have an onset in infancy. Neurologic symptoms develop in more than one-half of PNP deficient children. These neurologic problems include spastic diplegia or tetraparesis, ataxia, tremor, retarded motor development, hyper-or hypotonia, behavioral difficulties, and varying degrees of mental retardation. PNP deficiency also is associated with increased risk of autoimmune disorders, such as autoimmune hemolytic anemia, immune thrombocytopenia, neutropenia, thyroiditis, and lupus. Some of these patients developed cancer.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Purine nucleoside phosphorylase deficiency, eMedicine

Genetic:

- NP, IDdiagnostics

Therapeutic options:

- Treatment of infections with antibacterials, antifungals, and antivirals. Bone marrow transplantation. Other recommendations include: intravenous gamma-globulin infusion, irradiation of all blood products.
- Purine nucleoside phosphorylase deficiency, eMedicine

Research programs, clinical trials:

- Pilot Study of Allogeneic Bone Marrow Transplantation Plus Cyclosporine and Mycophenolate Mofetil to Induce Mixed Hematopoietic Chimerism in Patients With Primary T-Cell Immunodeficiency Disorders, ClinicalTrial.gov
- European Initiative for Primary Immunodeficiencies

GENE INFORMATION

Names:

HUGO name: NP
Alias(es): PNP, nucleoside phosphorylase, Purine nucleoside phosphorylase, Inosine phosphorylase

Localization:

Reference sequences:

DNA: M13953 (EMBL) , **cDNA:** X00737 (EMBL) , **Protein:** P00491 (SWISSPROT) Other Sequences

Chromosomal Location:

14q13.1

Maps:

NP (Map View)

Variations / Mutations:

- NPbase; Mutation registry for PNP deficiency

Other gene-based resources:

Ensembl: ENSG00000198805, GENATLAS: NP, GeneCard: NP, UniGene: 75514, Entrez Gene: 4860, euGenes: 4860, GDB: 120239

PROTEIN INFORMATION

Description:

Catalytic activity:

Purine nucleoside + phosphate = purine + alpha-d-ribose 1-phosphate

Subunit:

Homotrimer

Structures (PDB):

1ULA Application of crystallographic and modeling methods in the design of purine nucleoside phosphorylase inhibitors.

1ULB Application of crystallographic and modeling methods in the design of purine nucleoside phosphorylase inhibitors.

Other features:

Other related resourses:

PIR: PHHUPN, InterPro: IPR001369; Mtap_PNP, Pfam: PF00896; Mtap_PNP, PROSITE: PS01240; PNP_MTAP_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
umbilical cord vein, endothelium	25.22	2:346
omentum, greater omentum	15.75	1:277
skin, epithelium	12.43	1:351
fibrosarcoma	4.67	2:1867
germ cell, yolk sac	3.86	1:1129
pool, liver+spleen	1.99	28:61327
gall bladder	1.79	1:2435
whole blood	1.78	1:2445
stomach	1.70	43:110283
parathyroid	1.53	6:17083

Animal models:

Mouse:

MGD: ; Pnp

FlyBase:

euGenes: ; FlyBase

C. elegans:

euGenes: ; C. elegans

OTHER RESOURCES

Societies:

General:

- IPOPI, International Patient Organization for Primary Immunodeficiencies
- The Jeffrey Modell Foundation
- National Center for Biotechnology Information
- Immune Deficiency Foundation
- European Society for Immunodeficiencies

Disease specific:

- European Society for the Study of Purine and Pyrimidine Metabolism in Man, ESSPPMM
- The Purine Research Society
- The Purine Metabolic Patients Associations, PUMPA